NATIONAL MARROW DONOR PROGRAM®

BE THE MATCH®

April 29, 2013

LCDR Christopher Steele
Office of Naval Research
Code 34 – Warfighter Performance
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-13-1-0039 between the Office of Naval Research and the National Marrow Donor Program

Dear LCDR. Steele:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of December 1, 2012 to March 31, 2013.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at cabler@nmdp.org.

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Contracts Manager

Enclosure: Quarterly Report with SF298

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

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Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

Creating Connections. Saving Lives.™

Grant Award N00014-13-1-0039

DEVELOPMENT OF MEDICAL TECHNOLOGY FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY PERFORMANCE / TECHNICAL REPORT

FOR

DECEMBER 01, 2012 to MARCH 31, 2013

PERIOD 1

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
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IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

IIA.1 Task 1: Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event.

Period 1 Activity:

- Held Advanced Medical Response to a Radiological Disaster training session at the Radiation Emergency Assistance Center and Training Site in Oakridge, TN for 25 people including 4 physicians
- Continued to observe the Mayo Clinic's preparations for their RITN supported full scale radiological exercise to be held August 2013; this exercise will include the following three phases:
    - Phase I (8/16/13): Initial notification and activation of NDMS (Additionally, Phase I will include small-scale patient arrival to assess GS and ED's response plans.)
    - Phase II (8/26/13): NDMS triage: Tests communication, pre-arrival triage/placement decision making (including patient family care planning, in collaboration with community partners), activating surge plans, and potentially patient transfer planning/coordination activities between Mayo Clinic and Hospital Disaster Preparedness & Response Compact members.
    - Phase III (8/29/13): Full-Scale - activities similar to Phase II. Additionally, role-player/mannequin patients will be triaged, radiological surveys conducted, possible patient decontamination, and patient movement. Continued Hospital Emergency Operations Center (HICS Coordination Center) coordination activities with internal departments and external partners.
- RITN Medical Advisor activity; Dr. Weinstock participated in the following activities supporting the Radiation Injury Treatment Network:
    - He was an invited speaker at the Institutes of Medicine Improvised Nuclear Device Workshop in Washington, DC in January 2013
    - He organized the formation of a network of 18 RITN centers to participate in a G-CSF user managed inventory program, with a proposal submitted to BARDA for funding in January 2013
    - He assisted with the drafting of the 2013 RITN tabletop exercise

  - He helped with organization of the 2013 RITN/CMCR conference
  - He provided guidance to commercial entities (DxTerity, Sanofi) with interest in developing radiation countermeasures
  - He assisted with the recruitment of new RITN centers
  - He was invited to participate in a clinical guidance workshop in May 2013 organized by the Office of Policy and Planning, Division of Medical Countermeasure Strategy and Requirements, Department of Health and Human Services
  - He was invited to co-author the chapter on Nuclear and Radiological Events in KOENIG & SCHULTZ: Disaster Medicine, 2nd Edition
- Continued to develop relationships with the National Association of County and City Health Officials (NACCHO), the Association of State and Territorial Health Officials (ASTHO) and the Federal Emergency Management Agency (FEMA)
  - Participated in the National Association of City and County Health Officials (NACCHO) radiologically contaminated persons decontamination and quarantine legal review meeting in Atlanta
  - Participated in the preparations for the ASTHO-NARR contaminated traveler tabletop exercise in Seattle, WA
- Submitted the User Managed Inventory whitepaper to the Biomedical Advanced Research and Development Authority to increase preparedness at nationwide; this whitepaper we declined by BARDA for funding. However, BARDA committed to helping make appropriate connections with agencies that may fund the proposal.
- Continued to develop and release web based training modules for RITN, the following courses are released for use by RITN staff and RITN partners:
  - Introduction to RITN
  - Government Emergency Telecommunications Service (GETS) for RITN
  - Satellite Phone Training for RITN
  - Basic Radiation Training (BRT)
  - These two final courses are in the final stages of development with release anticipated for early summer 2013:

- RITN Concept of Operations
- Non-Medical Radiation Awareness Training

- Conducted three monthly RITN Center conference calls to review task completion status and allow a venue for centers to talk to peers

IIA.1 Task 2: *GCSF in Radiation Exposure – This task is closed.*

IIA.1 Task 3: *Patient Assessment Guidelines and System Enhancements – This task is closed*

IIA 1 Task 4: *National Data Collection Model – This task is closed.*

IIA. Contingency Preparedness – Objective 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.

IIA.2 Task 1: Ensure NMDP maintains effective plans to continue critical facility and staff-related functions as a result of operations interruption events.

Period 1 Activity:

- Managed the efforts by the Operations Group to prepare for and execute a planned 4-day IT outage of major systems to support a major software implementation. Led teams to determine what must be done to prepare for shutdown to include determining what activities to defer. Teams developed control reports, developed or refined manual processes for systems downtime, determine "Business Catch-up" needs, educated staff to effectively work the "new normal".
- Chaired daily consolidated meetings to increase crosstalk and to rapidly identify and resolve unanticipated issues due to system interdependencies. External partner feedback demonstrated the event was successfully transparent to external partners.
- Conducted tests of mass telephonic emergency notification system resulting in successfully contacting over 95% of staff with a prerecorded message.
- Conducted tests of the satellite telephones distributed to RITN centers to validate equipment accountability and user capability.

IIA.2 Task 2: *Sibling Typing Standard Operating Procedures – This task is closed*

IIA. Contingency Preparedness – Objective 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.

IIA.3 Task 1: *I.S. Disaster Recovery – This task is closed.*

IIA.3 Task 2: *Critical Facility and Staff Related Functions – This task is closed.*

IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

IIB.1 Task 1: Expand the genetic diversity of the Registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies.

Period 1 Activity:

Recruitment Typing

- 6 laboratories provided HLA typing on a total 72,658 newly recruited donors.
- The blind quality control testing error rate was 0.04%, meeting the project requirement of ≤ 2.0%.
- On-time testing completion rate was 98.9%, meeting the project requirement of a minimum of 90% of typing results reported within 14 days of shipment of samples.

HLA Mischaracterization Research

Alleles that are less common in the Be The Match Registry were evaluated to determine whether results may have been incorrectly reported based on rules established in previous typing projects. These rules include:

1. Alleles reported prior to 2004
2. Reported in a subject whose self described race is different than what was reported for the allele in the IMGT/HLA database

3. Rare alleles reported with another uncommon/rare allele
4. Alleles reported consistently with the same second allele.

74 samples were typed for intermediate HLA-A or B, 45 samples were typed at intermediate resolution DRB1. 48% of the HLA-A and B and 36% of the DRB1 samples were found to be incorrect. Samples previously typed at intermediate resolution where the suspicious allele was confirmed were then requested for high resolution SBT typing to verify the intermediate resolution typing methodology was able to correctly type this allele. High resolution typing was completed on 26 samples for HLA-A, 16 samples for HLA-B, and 31 HLA-DRB1. All samples typed at high resolution confirmed the intermediate resolution reporting.

2-Step Recruitment at Live Drive Registration:

The 2-Step recruitment project is evaluating a donor registration process that requires a subsequent activation step 24 hours after initial registration. The hypothesis is that this 2-step activation process can improve the commitment of newly recruited donors and increase availability. A Phase One pilot was completed to demonstrate feasibility of the process, but did not generate sufficient data to determine whether the process should be fully operationalized. Therefore, a Phase Two pilot was launched to generate more data.

- The 2-Step Activation Phase Two Pilot launched on March 28, 2013 and will run for 3 months.
- An online activation channel was added, in addition to the Phase One channels of phone and text activation.
- The pilot launched without issue and is off to a fast start. More than 60 drives have already been scheduled and new recruit activations are being received.

IIB.1 Task 2: *Evaluate HLA-DRB1 High Res typing – This task is closed.*

IIB.1 Task 3: *Evaluate HLA-C Typing of Donors – This task is closed*

IIB.1 Task 4: Evaluate the suitability of buccal swabs as a method to collect DNA samples to HLA type casualties and potential related donors in contingency situations, and to obtain research samples.

Period 1 Activity:

- **Alternate Sample Collection Methods:** Initial discussions were held with an expert on biological sample preservation, regarding simple treatments with potential for protecting DNA integrity on buccal swabs stored at room temperature or frozen conditions. A consulting agreement will be put in place in the next period, for this expert to create a feasibility report covering current methodologies and potential approaches to improve long term stability of samples.

IIB 1 Task 5: Evaluate the factors of donor utilization and speed of search process after strategic upgrading of selected adult volunteer donors.

Period 1 Activity:

- **Investigate CMV or ABO testing from alternative sample types:** ABO testing is more likely to be feasible than CMV, and would have a similar benefit in providing early information to speed the search process for some patients.
    - CMV testing from saliva samples is unlikely to be suitable to allow a correlation to presence/absence of CMV antibody. A 2013 study by Descamps *et al.* using the Oragene saliva kit showed that CMV shedding was insufficient for PCR assay detection.
    - A working group was formed to investigate multiple channels for acquiring registry member ABO Rh information for registry listing, prior to determination of blood type from a fresh blood sample at the Confirmatory Typing stage. Avenues include gathering member self-reported blood type and potential for utilizing a simple ABO Rh home test kit.

IIB 1 Task 6: Maintain a comprehensive quality control program.

Period 1 Activity:

- No activity this period.

IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.

IIB 2 Task 1: Ongoing collection of primary data for validation and storage in the Registry database.

Period 1 Activity:

- No activity this period.

IIB 2 Task 2: *Validation of Logic of Primary Data – This task is closed.*

IIB 2 Task 3: *Reinterpretation of Primary Data – This Task has been merged with Task IIB2.4.*

IIB 2 Task 4: Interpretation of the primary data into genotype lists and integration into matching algorithm to optimize placement of donors onto patient searches.

Period 1 Activity:

- Performed interpretation on primary data into GL Strings for HLA DB Versions 3.8.0 and 3.11.0. Reinterpretation pipeline has been re-engineered to re-analyze the full registry data of >20 million locus-levels results within 24 hours.
- Deployed a new version of the Silver Standard genotype list RESTful web service for IMGT/HLA Database nomenclature versions 3.11.0 at http://gl.immunogenomics.org/imgt-hla/3.11.0/.
- HL7:
    - Participated in the HL7 Working Group Meeting in Phoenix AZ, Jan 14-18 on working groups for Clinical Genomics, Structured Documents, and Orders & Observations. The Genetic Testing Report passed Draft Standard for Trial Use (DSTU) balloting.
    - Participated in weekly Clinical Genomics Workgroup meetings. Continued to develop constrained CDA for reporting HLA typing.
- Genetic Testing Registry (GTR), Continued discussions with Mike Feolo and NCBI staff to develop use of NCBI GTR for meeting Silver Standard principles for methodology reporting of HLA typing. Agreements signed between NCBI and One Lambda for including One Lambda data into NCBI GTR. Received spreadsheets for RSSOH2B1 lot 008 and RSSO2B1 lot 017 kits which will be used for the pilot.

IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

IIB.3 Task 1: Incorporate HLA allele and haplotype frequencies into matching algorithm.

Period 1 Activity:

- No activity this period.

IIB 3 Task 2: Continue to enhance the allele and haplotype frequency data to include additional loci and increased resolution for ethnic groups with input from consultants with expertise in population genetics.

Period 1 Activity:

- Worked progressed toward generating HLA Haplotype Frequencies based on the genomic allele names which will allow the identification of associations that are currently ignored for applications of this data to matching such as:
  - C*16:01~B*52:01:02
  - C*03:03:01G~B*52:01:02
  - C*12:02:01G~B*52:01:01G
- Resubmitted new haplotype frequency manuscript “Six-Locus High Resolution HLA Haplotype Frequencies Developed for Mixed-Resolution DNA Typing for the Entire US Donor Registry” based on minor comments from reviewers. Manuscript is expected to be published in Human Immunology late summer.
- Resubmitted new manuscript summarizing IHIW project “Comparative Validation of Computer Programs for Haplotype Frequency Estimation from Donor Registry Data” based on minor comments from reviewers. Manuscript is expected to be published in Tissue Antigens in late summer.

IIB 3 Task 3: Cord Blood and Adult Donor Matching Benchmarks and Registry Modeling.

Period 1 Activity:

- Ancestry Questionnaire Project (AQP)
  - We have revised the protocol for the AQP project and received IRB approval.
  - We have performed preliminary analysis of the first data pull for the AQP study, determining that there is a significant difference between subjects’ initial self-identified race and ethnicity (SIRE) response and those obtained from the test questionnaires.
- Met in Leiden to discuss NIMA (Non-Inherited Maternal Antigen) modeling with Professor van Rood, and completed modeling to a level where a manuscript is in preparation, entitled " Modeling NIMA Match Rates for Be the Match Registry® ".

IIB 3 Task 4: Couple haplotype prediction methodology with donor demographic data to target recruitment to areas populated by individuals with underrepresented HLA phenotypes.

Period 1 Activity:

- IMMPUTE project;
  - We have standardized the format of 1000 Genomes (1KG) HLA genotype data for distribution to collaborators
  - We have further developed the experimental plan for this project in conjunction with our collaborators at UCSF and CHORI. We have extended this plan to include a set of data-requirements for IMMPUTE collaborators to ensure analytical consistency in downstream analyses. We have also developed a methodological survey to be distributed to all IMMPUTE collaborators.
- We have rewritten, expanded and revised the introduction to the GL String manuscript in anticipation of its submission for publication.
- We have worked with Drs. Hollenbach, Fernandez-Vina and Scott Conradson to plan the second NGS Data consortium meeting to be held in conjunction with the European Federation for Immunogenetics (EFI) meeting in May.
- Validation of 5-locus imputation and a new method for estimation of synthetic Haplotype Frequencies (SHF) on simulated data showed promising results. Further validation is underway on registry data.
- Implement very simple GL string "parsing" and then run imputation on NEMO2012 HR simulated cohort using NEMO2011 plus SHF
- Created simulated datasets of HLA typing at varying resolutions for validation of 5-locus imputation algorithm and synthetic haplotype frequencies and objective comparison of HLA typing resolution.

IIB 3 Task 5: Develop a bioinformatics web site for frequency information.

Period 1 Activity:

- No activity this period.

IIB 3 Task 6: Use NMDP's expert Search Strategy Advisors as resources to further improve the matching algorithm and donor/cord blood identification software applications with the goal to maximize the ability of the software to identify the best donors/cords for each patient.

Period 1 Activity:

- No activity this period.

IIB 3 Task 7: *Population Genetics – This task was merged with Task IIB3.2*

IIB 3 Task 8: *Haplotype Matching – This task was merged with Task IIB3.2*

IIB 3 Task 9: *Global Haplotype/Benchmark – This task was merged with Task IIB3.3*

IIB. Rapid Identification of Matched Donors – Objective 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

IIB.4 Task 1: *Expand Network Communications – This task is closed.*

IIB.4 Task 2: Conduct a study of random patient search simulations to test the efficacy of centralized contingency management.

Period 1 Activity:

- NMDP provided support for donor/cord blood unit identification, selection and collection for the NIH intramural unrelated donor transplant program. Activity in the last quarter was as follows:
  - 5 formal searches
  - 21 donor confirmatory typing blood sample and IDM testing requests
  - 4 cord blood unit confirmatory typing requests
  - 3 PBSC collections and 1 therapeutic T cell collection
- CIBMTR provided support for rapid identification of potential donors for newly diagnosed AML patients under the

following clinical trial protocol:

- S1203: A Randomized Phase III Study of Standard Cytarabine plus Daunorubicin (7+3) Therapy or Idarubicin with High Dose Cytarabine (IA) versus IA with Vorinostat (IA+V) in Younger Patients with Previously Untreated Acute Myeloid Leukemia (AML)
- CIBMTR provides study-specific sample collection kits for patients, processes samples, arranges HLA typing, and generates preliminary search strategy reports to assist in the identification of donors and/or CBU through the NMDP.
- It is anticipated that 750 patients will be accrued in less than 5 years with 40% needing HLA testing and search strategy results. The trial is scheduled to open early next quarter.

IIB.4 Task 3: *Benchmarking Analysis – This task is closed*

IIB.4 Task 4: *Expand Capabilities of Collection and Apheresis Centers – This task is closed.*

IIC. Immunogenetic Studies – Objective 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.

IIC.1 Task 1: Continue to evaluate HLA disparity and impact on HSC transplantation by adding selected pairs to the Donor/Recipient Pair project utilizing sample selection criteria that optimize the new data generated by the typing project.

Period 1 Activity:

Donor Recipient Pair Project
In 1994 a retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. Presence/absence typing of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1) has been included.

SG30 period of performance came to a close on September 30th, 2012. Audit of KIR has continued.

- SG31 period of performance came to a close on December 31th, 2012. SG 31 consisted of 168 single cord blood transplants

and 33 double cord blood transplants. This is the first sample group with double cord transplants. The audit process is ongoing.

- KIR discrepancy and no make resolution have continued.
- To date over 6000 samples have been typed for presence/absence of 14 KIR loci (2DL1-5, 2DS1-5, 3DL1-3 and 3DS1).
- A project has been initiated to add the pseudo genes, 2DP1 and 3DP1, into the IPR database. NMDP housed data has been uploaded into the database and the remaining sample types are being requested from the typing laboratories.

Current HLA matching guidelines for unrelated HCT recommend avoidance of mismatches only within the Antigen Binding Domain (ABD). This recommendation is based on the hypothesis that amino acid differences outside the ABD are not immunogenic. The ABD allo-reactivity assessment project will give insight into the allowable percent tolerance of matching needed outside of the ABD.

- Previously investigated data from Class II non-ABD mismatched were written up and submitted to the EFI 2013 conference and has been selected for an oral presentation.
- Further investigation of the Class II non-ABD mismatched DRB1*14:01:01 and DRB1*14:54 have continued. Queries of DRB1*14:01:01/14:54 haplotypes have resumed to identify additional registry member that may be included in the study.
- Initial investigation of the class I non-ABD mismatches (A*02:01/02:09, B*44:02/44:27 and C*07:01/07:06) have been performed where both alleles have been seen in the same genotype. Specific queries of the Be The Match Registry allowed for selection of one hundred and forty potential donors to be typed at high resolution for the class I locus of interest. Further typing of haplotypes potentially carrying either Class I C*07:01/07:06 or 07:01/07:18 was performed. Analysis of this data is still ongoing.

IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

IIC.2 Task 1: Continue to develop typing protocols for non-HLA immunogenetic loci, development of a lab network, enhancement of database to capture non-HLA data and continue analyses to evaluate genetic diversity in the transplant population.

Period 1 Activity:

- No activity this period.

IIC 2 Task 2: *Related Pairs Research Repository – This task is closed.*

IIC 2 Task 3: *CIBMTR Integration – This task is closed.*

IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

IID.1 Task 1: Conduct observational research and interventional clinical trials.

Period 1 Activity:

Testing was completed for the validation phase for the study investigating biomarkers associated with cord blood engraftment in order to ensure the generation of consistent results at both testing sites of Duke and SLCBB. Testing involved the following:

- Five new segments from five different cord blood units (CBU) processed at St. Louis Cord Blood Bank (SLCBB) were tested.
- 29 segments from 29 different CBUs were tested by SLCBB. These 29 segments were part of the initial validation between Duke and MDACC. Therefore the results already exist for Duke. The data from Duke was compared to SLCBB.

Inter-laboratory results specifically for the target cells of interest (ALDHbr %CD45 viable cells) were as follows:

Dataset (# of segments tested at each site)	Measurement	Subject variance	Within subject variance	Reliability
(N=5)	ALDHbr (% viable CD45)	0.059	0.016	**78.8%**
(N=29)	ALDHbr (% viable CD45)	0.062	0.033	**65.4%**

The reliability of both data sets did not satisfy the pre-established acceptability threshold of ≥ 80%. An investigation into the possible areas where inter-laboratory variation was being introduced with involve the following next steps:

- The two laboratories will swap raw flow cytometry data and re-gate.
- Once re-gating is complete, histograms from each lab will be compared side-by-side to look for variance in gating strategies.
- Run reliability analysis for between SLCBB and MDACC datasets for the 29 segments tested.

Results will be reported in the next quarter.

Work continued on the development of the anti-HLA donor specific antibody study of recipients transplanted with CBUs.

- Potential pairs eligible for inclusion in the study were identified.
- Next steps include finalizing cohorts and identifying graft failure cases.

Work continued on a study to assess CBU characteristics (viability, TNC, CFU and CD34) pre-freeze and post thaw.

- The study proposal was presented to the Graft Sources and Manipulation Working Committee meeting during Tandem 2013. The committee members assigned a low priority score and were unable to accept the proposal.
- The Cord Research Subcommittee met to discuss the future of the study and determined to continue without the support of the Graft Sources and Manipulation Working Committee.
- Further protocol development based on suggestions made by the Graft Sources and Manipulation Working Committee as well as defined data points to capture will be determined during the next quarter.

Prospective Studies; RCI BMT

- During this quarter, monitoring activities continued at participating donor centers for the PBSC vs. Marrow clinical trial.
- Staff continued to coordinate, manage data collection and monitor sites related to the Adult Double Cord trial.
- Activities continued on the Long Term Donor Follow up project. During this reporting period we reached an accrual of 10,500 donors. Donor Centers continue to actively perform consent sessions with donors during their standard work-up process.
- Database management updates were made to the AdvantageEDC^{SM} system used for both the Double Cord and Revelimid

trials.

- Activities continued on the Long Term Donor Follow up project. Survey Research Group (SRG) staff made outreach to accrued donors whose follow-up time point became due during this quarter and that they are responsible. A total of 1179 donors were reached and data form completed. Donor Centers continue to actively perform consent sessions with donors during their standard work-up process. During this reporting period overall accrual reached almost 14,700 donors which is 46% of the accrual goal of 32,128. The enrollment is broken down into ~9,200 donors who donated prior to Oct. 2010 and ~7,500 donor donating after trial activation.
- The RCI BMT Clinical Trials Advisory Committee held a meeting at the February Tandem Meetings. During this meeting activities within the RCI BMT were reviewed and no new proposals were reviewed.

Information Technology:

FormsNet

Additional accomplishments were made in delivering new functionality, improving data quality, data capture and data reporting through the CIBMTR IT suite of applications.

The second FormsNet upgrade project, which will upgrade the Donor module to FormsNet 3, is nearing the end of the Analysis phase. The first development iteration is underway. The team continues to use the Agile methodology, which provides frequent opportunities for the business to view and test the deliverables/system.

The FormsNet3 / AGNIS Integration release successfully implemented in March 2013. The primary objective of the integration release was to enable partners submitting data through AGNIS to be fully live on the FormsNet 3 platform. The release also included some key FormsNet 3 enhancements.

A release is underway to automate the monitoring of a clinical trial; this release is in the process of testing.

AGNIS

- Released support of forms 2018, 2118 (Lymphoma Disease forms) - (7/31)
- Production submission available for EBMT to submit forms 2400 and 2804. Working to expand 2400 diseases for submission and EBMT center data sharing agreements. Estimate of 2000 records to be received by 7/31

- Continue to support EBMT efforts for bulk form submission
- Cleveland Clinic has requested permission for 2900 production submission.
- Remedy Md is submitting forms 2900, 2804, 2400, and 2450 in production for University of Utah. Development efforts to submit other forms and to retrieve forms underway.
- 20 StemSoft centers retrieving data.

IID.1 Task 2: *Research with NMDP Donors – This task was merged with IID1.1.*

IID.1 Task 3: Expand support for immunobiology research, statistical genetics and clinical research studies under CIBMTR Immunobiology Working Committee.

Period 1 Activity:

The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies.

The annual IBWC meeting was held at the BMT Tandem meetings in Salt Lake City in February. All IBWC members were invited to attend and provided the opportunity to present updates on ongoing studies. In addition, the group reviewed new study proposals, assigns priority with full committee feedback and plans the scientific agenda/work plan for the 2013-2014 academic year. Ten new proposals were submitted for review. Nine were accepted and one was combined with an ongoing study.

- 9 new proposals were accepted:
  - Reza Abdi, Gil Alterovitz and David McDermott, *Interaction between SNPs and clinical data using predictive modeling on a Bayesian network framework/ Short and long term survival assessment of post HSCT transplantation using predictive modeling on a Bayesian network framework.*
  - Medhat Askar and Ron Sobecks, *The Impact Of MHC Class I Chain-Related Gene A (MICA) Donor-Recipient Mismatches and MICA-129 Polymorphism On Unrelated Donor Hematopoietic Stem Cell Transplants (HSCT) For Hematological Malignancies.*
  - Yorum Louzoun, *The development of Machine Learning based classifiers to define the alloreactivity of HLA mismatches in unrelated donor hematopoietic stem cell transplantation.*
  - Paul Veys and Mary Eapen, *The effect of allele-level HLA-matching on survival after umbilical cord blood transplantation for non-malignant diseases in children.*

- Adam Gassas and Jane Danska, *Impact of donor signal-regulatory protein alpha (SIRPα) polymorphism on outcome of allogeneic hematopoietic stem cell transplantation (allo-HCT).*
- Susana Marino, *Effects of HLA Class I Amino Acid Mismatches on Stem Cell Transplant Outcomes.*
- Adam Lazaryan, *Significance of HLA class I and II allelic mismatching within and outside of HLA supertypes among recipients of single-allele mismatched unrelated allogeneic hematopoietic stem cell transplantation: A CIBMTR and NMDP Research Study.*
- John Harvey and Vanderson Rocha, *Discrepancy analysis of microsatellite loci as a proxy measure for ancestral differentiation between donors and recipients: correlation between high scores and poorer overall survival in high resolution matched unrelated donor transplantation.*
- Vahid Afshar-Khargan, *Role of the complement system in graft-versus-host disease.*

- 1 new proposal combined with an existing study:
  - Johannes Fischer, *Effect of HLA-C allele matching in the context of recipient HLA-C-encoded KIR ligand grouping (C1 or C2) on the outcome of unrelated hematopoietic stem cell transplantation.* Combined with IB12-04 led by Jeff Venstrom.
- One abstract was presented:
  - Craig Kollman, et al., *The effect of donor characteristics on raft vs. host disease and survival after unrelated donor transplantation for hematologic malignancy.* Oral presentation – 2013 BMT Tandem Meetings
- Two manuscripts were submitted:
  - Marcelo Fernandez-Vina, et al., *Multiple mismatches at the low expression HLA loci DP, DQ, DRB3/4/5 associate with adverse outcomes in hematopoietic stem cell transplantation.* Submitted to Blood
  - Carolyn K Hurley, et al., *The impact of HLA unidirectional mismatches on the outcome of myeloablative hematopoietic stem cell transplantation with unrelated donors.* Submitted to Blood
- Two manuscripts were published:
  - Christiane Dobbelstein, et. al, *Birth order and transplant outcome in HLA-identical sibling stem cell transplantation – an analysis on behalf of the CIBMTR.* BBMT Feb 1, 2013 [Epub ahead of print]

- Effie Petersdorf, et al., *Increasing the safety of HLA-mismatched unrelated donor hematopoietic transplantation.* Blood Jan 10, 2013 [Epub ahead of print]

ACRONYM LIST

AABB	American Association of Blood Banks	HR	High Resolution
AFA	African American	HRSA	Health Resources and Services Administration
AGNIS	A Growable Network Information System	HSC	Hematopoietic Stem Cell
AML	Acute Myelogenous Leukemia	IBWC	Immunobiology Working Committee
ABD	Antigen Binding Domain	IDM	Infectious Disease Markers
API	Asian Pacific Islander	IHWG	International Histocompatibility Working Group
AQP	Ancestry Questionnaire Project		
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IPR	Immunobiology Project Results
ASBMT	American Society for Blood and Marrow Transplantation	ICRHER	International Consortium for Research on Health Effects of Radiation
ASHI	American Society for Histocompatibility and Immunogenetics	IND	Investigational New Drug
ASTHO	Association of State and Territorial Health Officials	IS	Information Services
B-LCLs	B-Lymphoblastoid Cell Lines	IT	Information Technology
BARDA	Biomedical Advanced Research and Development Authority	IRB	Institutional Review Board
BBMT	Biology of Blood and Marrow Transplant	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BCP	Business Continuity Plan	KIR	Killer Immunoglobulin-like Receptor
BCPeX	Business Continuity Plan Exercise	MDACC	MD Anderson Cancer Center
BMCC	Bone Marrow Coordinating Center	MDS	Myelodysplastic Syndrome
BMDW	Bone Marrow Donors Worldwide	MHC	Major Histocompatibility Complex
BMT	Bone Marrow Transplantation	MICA	MHC Class I-Like Molecule, Chain A
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICB	MHC Class I-Like Molecule, Chain B
BODI	Business Objects Data Integrator	MKE	Milwaukee
BRT	Basic Radiation Training	MRD	Minimal Residual Disease
C&A	Certification and Accreditation	MSKCC	Memorial Sloan-Kettering Cancer Center

CAU	Caucasian	MSP	Minneapolis
CBMTG	Canadian Blood and Marrow Transplant Group	MUD	Matched Unrelated Donor
CBB	Cord Blood Bank	NAC	Nuclear Accident Committee
CBC	Congressional Black Caucus	NCBI	National Center for Biotechnology Information
CBS	Canadian Blood Service	NCBM	National Conference of Black Mayors
CBU	Cord Blood Unit	NACCHO	National Association of County & City Health Officials
CDA	Clinical Document Architecture	NARR	National Alliance for Radiation Readiness
CFU	Colony Forming Unit	NCI	National Cancer Institute
CHORI	Children's Hospital of Ockland Research Institute	NDMS	National Disaster Medical System
CHTC	Certified Hematopoeitic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CIBMTR	Center for International Blood & Marrow Transplant Research	NGS	Next Generation Sequencing
CIT	CIBMTR Information Technology	NHLBI	National Heart Lung and Blood Institute
CLIA	Clinical Laboratory Improvement Amendment	NIH	National Institutes of Health
CMCR	Centers for Medical Countermeasures against Radiation	NIMA	Non-Inherited Maternal Antigen
CME	Continuing Medical Education	NIMS	National Incident Management System
CMF	Community Matching Funds	NK	Natural Killer
CMV	Cytomegalovirus	NLE	National Level Exercise
COG	Children's Oncology Group	NMDP	National Marrow Donor Program
CREG	Cross Reactive Groups	NRP	National Response Plan
CSS	Center Support Services	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CT	Confirmatory Testing	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CTA	Clinical Trial Application	OIT	Office of Information Technology
DC	Donor Center	OMB	Office of Management and Budget
DHHS-ASPR	Department of Health and Human Service –	ONR	Office of Naval Research

	Assistant Secretary Preparedness and Response		
DIY	Do it yourself	P2P	Peer-to-Peer
DKMS	Deutsche Knochenmarkspenderdatei	PBMC	Peripheral Blood Mononuclear Cells
DMSO	Dimethylsulphoxide	PBSC	Peripheral Blood Stem Cell
DoD	Department of Defense	PCR	Polymerase Chain Reaction
DHHS-ASPR	Department of Health and Human Services – Assistant Secretary for Preparedness and Response	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
DSTU	Draft Standard for Trial Use	REAC/TS	Radiation Emergency Assistance Center/Training Site
EBMT	European Group for Blood and Marrow Transplantation	REST	Representational State Transfer
ED	Emergency Department	RFP	Request for Proposal
EDC	Electronic Data Capture	RFQ	Request for Quotation
EFI	European Federation of Immunogenetics	RG	Recruitment Group
EM	Expectation Maximization	RITN	Radiation Injury Treatment Network
EMDIS	European Marrow Donor Information System	SBT	Sequence Based Typing
ENS	Emergency Notification System	SCTOD	Stem Cell Therapeutics Outcome Database
ERSI	Environment Remote Sensing Institute	SG	Sample Group
FBI	Federal Bureau of Investigation	SHF	Synthetic Haplotype Frequency
FDA	Food and Drug Administration	SLCBB	St. Louis Cord Blood Bank
		SLW	STAR Link® Web
FDR	Fund Drive Request	SSA	Search Strategy Advice
FLOCK	Flow Cytometry Analysis Component	SSO	Sequence Specific Oligonucleotides
Fst	Fixation Index	SSP	Sequence Specific Primers
GETS	Government Emergency Telecommunications Service	SSOP	Sequence Specific Oligonucleotide Probes
GCSF	Granulocyte-Colony Stimulating Factor (also	STAR®	Search, Tracking and Registry

	known as filgrastim)		
GIS	Geographic Information System	TC	Transplant Center
GS	General Services	TED	Transplant Essential Data
GTR	Genetic Testing Registry	TNC	Total Nucleated Cell
GvHD	Graft vs Host Disease	TSA	Transportation Security Agency
HCS	HealthCare Standard	UCSF	University of California – San Francisco
HCT	Hematopoietic Cell Transplantation	UI	User Interface
HEPP	Hospital Emergency Preparedness Program	UML	Unified Modeling Language
HHQ	Health History Questionnaire	URD	Unrelated Donor
HHS	Health and Human Services	WGA	Whole Genome Amplification
HIPAA	Health Insurance Portability and Accountability Act	WMDA	World Marrow Donor Association
HIS	Hispanic	WU	Work-up
HLA	Human Leukocyte Antigen		
HML	Histoimmunogenetics Mark-up Language		